

Implementing Pragmatic Trials via Electronic Platforms: Practical and Ethical Considerations for Consent, Participation, and Analysis

Andrea B. Troxel, Sc.D.

Department of Population Health
Division of Biostatistics
NYU Grossman School of Medicine

May 26, 2021

Colorado Pragmatic Research in Health Conference

not for reproduction without permission



Overview

Pragmatic Trials

Digital Platforms

Examples

EMPOWER

BE-EHR

Summary

Overview

Pragmatic Trials

Digital Platforms

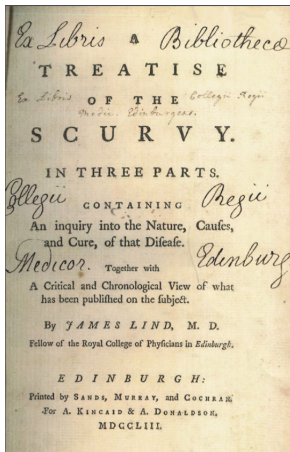
Examples

EMPOWER

BE-EHR

Summary

An early pragmatic trial



An early pragmatic trial

The following are the experiments.

On the 20th of *May* 1747, I took twelve patients in the scurvy, on board the *Salisbury* at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees. They lay together in one place, being a proper apartment for the sick in the fore-hold; and had one diet common to all, *viz.* water-gruel sweetened with sugar in the morning; fresh mutton-broth often times for dinner; at other times puddings, boiled biscuit with sugar, &c.; and for supper, barley and raisins, rice and currants, figs and wine, or the like. Two of these were ordered each a quart of cyder a-day. Two others took twenty-five guts of *elixir vitriol* three times a-day, upon an empty stomach; using a gargle strongly acidulated with it for their mouths. Two others took two spoonfuls of vinegar three times a-day, upon an empty stomach; having their gruels and their other food well acidulated with it, as also the gargle for their mouth. Two of the worst patients, with the tendons in the ham rigid, (a symptom none of the rest had), were put under a course of sea-water. Of this they drank half a pint every day, and sometimes more or less as it operated, by way of gentle physic. Two others had each two oranges and one lemon given them every day. These they eat with green

herbs, at different times, upon an empty stomach. They continued but six days under this course, having consumed the quantity that could be spared. The two remaining patients, took the bigness of a nutmeg three times a-day, of an electuary recommended by an hospital-physician, made of garlic, mustard-seed, *rad. raphan.* balsam of *Peru*, and gum myrrh; using for common drink, barley-water well acidulated with tamarinds; by a decoction of which, with the addition of *cremor tartar*, they were gently purged three or four times during the course.

The consequence was, that the most sudden and visible good effects were perceived from the use of the oranges and lemons; one of those who had taken them, being at the end of six days fit for duty. The spots were not indeed at that time quite off his body, nor his gums found; but without any other medicine, than a gargle of *elixir vitriol*, he became quite healthy before we came into *Plymouth*, which was on the 16th of *June*. The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick.

Four common features of pragmatic clinical trials

- diverse, unselected patient population
 - ▶ limited eligibility criteria
 - ▶ recruitment from diverse settings
 - ▶ low barriers to enrollment
- simple, clinically relevant interventions
 - ▶ require no specialized expertise to implement
 - ▶ widely scalable
- simple, easily measured outcomes
 - ▶ require no specialized processes to obtain
 - ▶ come from existing sources
- non-standard randomization structures
 - ▶ cluster randomization
 - ▶ unbalanced randomization ratios

Four common features of pragmatic clinical trials

- diverse, unselected patient population
 - ▶ limited eligibility criteria
 - ▶ recruitment from diverse settings
 - ▶ low barriers to enrollment
- simple, clinically relevant interventions
 - ▶ require no specialized expertise to implement
 - ▶ widely scalable
- simple, easily measured outcomes
 - ▶ require no specialized processes to obtain
 - ▶ come from existing sources
- non-standard randomization structures
 - ▶ cluster randomization
 - ▶ unbalanced randomization ratios

Four common features of pragmatic clinical trials

- diverse, unselected patient population
 - ▶ limited eligibility criteria
 - ▶ recruitment from diverse settings
 - ▶ low barriers to enrollment
- simple, clinically relevant interventions
 - ▶ require no specialized expertise to implement
 - ▶ widely scalable
- simple, easily measured outcomes
 - ▶ require no specialized processes to obtain
 - ▶ come from existing sources
- non-standard randomization structures
 - ▶ cluster randomization
 - ▶ unbalanced randomization ratios

Four common features of pragmatic clinical trials

- diverse, unselected patient population
 - ▶ limited eligibility criteria
 - ▶ recruitment from diverse settings
 - ▶ low barriers to enrollment
- simple, clinically relevant interventions
 - ▶ require no specialized expertise to implement
 - ▶ widely scalable
- simple, easily measured outcomes
 - ▶ require no specialized processes to obtain
 - ▶ come from existing sources
- non-standard randomization structures
 - ▶ cluster randomization
 - ▶ unbalanced randomization ratios

Four common features of pragmatic clinical trials

- diverse, unselected patient population
 - ▶ limited eligibility criteria
 - ▶ recruitment from diverse settings
 - ▶ low barriers to enrollment
- simple, clinically relevant interventions
 - ▶ require no specialized expertise to implement
 - ▶ widely scalable
- simple, easily measured outcomes
 - ▶ require no specialized processes to obtain
 - ▶ come from existing sources
- non-standard randomization structures
 - ▶ cluster randomization
 - ▶ unbalanced randomization ratios

Pragmatic trials: A definition

Califf RM and Sugarman J (2015). Exploring the ethical and regulatory issues in pragmatic clinical trials. *Clin Trials* 12: 436-41.

1. An intent to **inform decision makers** rather than **elucidate a mechanism**
2. An intent to enroll a population **relevant** to the decision and **representative** of the group for whom the decision is relevant
3. An intent to either
 - 3.1 **streamline** procedures and data collection to provide adequate power
 - 3.2 measure a **broad range of outcomes**

Pragmatic trials and behavioral interventions

- Effect of selection in a trial
 - ▶ trial of drug
 - ▶ trial of behavioral intervention
- Drug trial
 - ▶ biological mechanism of action
 - ▶ unaffected by patient selection?
- Behavioral trial
 - ▶ participant motivation affects enrollment
 - ▶ participant motivation affects response to intervention
- Standard RCTs may provide high confidence answers to the wrong question

Overview

Pragmatic Trials

Digital Platforms

Examples

EMPOWER
BE-EHR

Summary

A rapidly changing environment

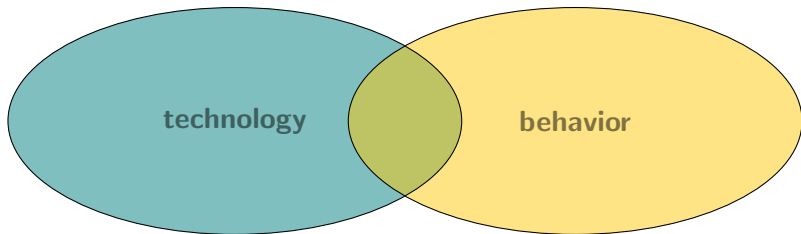
- Technology
 - ▶ computers are larger, faster, and more efficient than ever
 - ▶ smartphones and tablets are prevalent
 - ▶ proliferation of wearable devices
- Changes in health care delivery
 - ▶ virtual care

Health information

- Electronic health records
 - ▶ outpatient
 - ▶ inpatient
 - ▶ specialty services
- Claims information
- Registry information
- Social media

Scalability

- Scale is impossible without technology
- Technology is useless unless it engages human behavior



Digital platforms

- Trial implementation
 - ▶ randomization
 - ▶ participant scheduling and tracking
 - ▶ trial activity tracking
 - ▶ safety monitoring
 - ▶ DSMB reporting
- Device linkage
- Participant outreach
 - ▶ ecological momentary assessment
 - ▶ text communication
 - ▶ platform-enabled surveys
- Communication
 - ▶ patient-facing
 - ▶ provider-facing

EHR-based platforms

- Trial implementation
 - ▶ basic randomization
 - ▶ participant scheduling and tracking
 - ▶ safety monitoring
- Device linkage
- Participant outreach
 - ▶ text communication
 - ▶ platform-enabled surveys
- Communication
 - ▶ patient-facing
 - ▶ provider-facing

Overview

Pragmatic Trials

Digital Platforms

Examples

EMPOWER

BE-EHR

Summary

Examples

- EMPOWER
- BE-EHR

EMPOWER

- Electronic Monitoring of Patients Offers Ways to Enhance Recovery
- Pragmatic RCT in patients with CHF

Mehta SJ, Volpp KG, Asch DA, Goldberg LR, Russell LB, Norton LA, Iannotti LG, Troxel AB. 2019. Rationale and design of EMPOWER, a pragmatic randomized trial of automated hovering in patients with congestive heart failure. *Circulation: Cardiovascular Quality and Outcomes* 12: 005126.

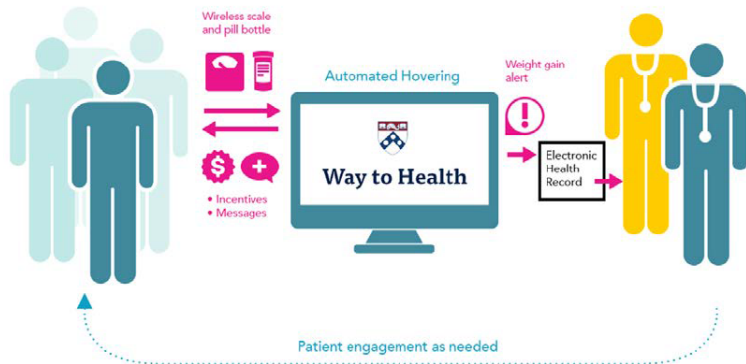
EMPOWER

- Intervention
 - ▶ lottery for patients to incentivize
 - ▶ daily weigh-ins
 - ▶ daily adherence to diuretics
 - ▶ wireless devices
 - ▶ scale
 - ▶ pill bottle
 - ▶ alerts to providers of substantial weight gain
 - ▶ more than 3 pounds in 24 hours
 - ▶ more than 5 pounds in 72 hours

EMPOWER

EMPOWER

EMPOWER



EMPOWER

- Intervention delivered electronically
 - ▶ daily engagement of patients
 - ▶ extra communication when triggered by automated data
- Embedded within the health system
 - ▶ incorporate into existing clinical workflow
 - ▶ minimize burden on busy clinicians
 - ▶ enhance management within context of care
- Traditional in-person informed consent
- Outcomes measured using EHR data
 - ▶ hospitalizations
 - ▶ primary diagnoses

BE-EHR

- Behavioral Economics in the Electronic Health Record
- Pragmatic RCT in older patients with diabetes

Belli HM, Chokshi SK, Hegde R, Troxel AB, Blecker S, Testa PA, Anderman J, Wong C, Mann DM. 2020. Implementation of a behavioral economics electronic health record (BE-EHR) module to reduce overtreatment of diabetes in older adults. *Journal of General Internal Medicine* 35(11): 3254-61.

BE-EHR

- Nudges to providers embedded within the EHR
 - ▶ tailored advisory
 - ▶ refill protocol
 - ▶ lab result

BestPractice Older Adult Guidelines Meds & Orders SmartSets

Older Adult Guidelines (1)

Attention - Target A1C is Different for Patients Over 75!

Based on the patient's active problems, visit diagnoses, and age, a HIGH life expectancy has been calculated.

Guidelines for this patient:
High life expectancy → A1C target = 7.0 - 7.5%

Patient's most recent A1C:
HEMOGLOBIN A1C, POC (%)

Date	Value	Status
04/02/2019	6 (A)	Final

No results found for: HGBA1C

Tighter control can lead to dizziness, confusion, and other problems from hypoglycemia.

Consider joining your colleagues by:

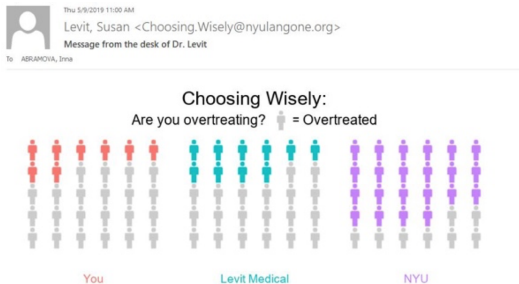
- Reducing current diabetes medication

[Life Expectancy Algorithm](#)
[Choosing Wisely Guidelines](#)
[Jump to Orders](#)

Acknowledge Reason

BE-EHR

• Peer comparison emails



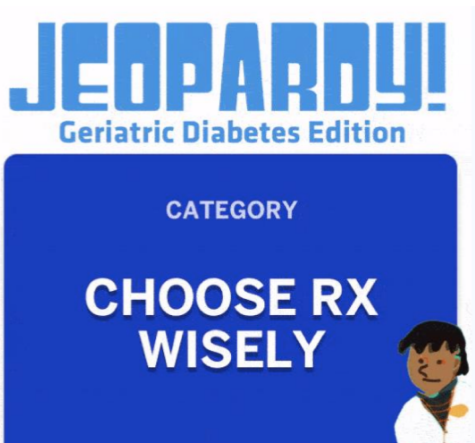
You are receiving this message because you have seen a patient age 76 or older with diabetes in the last month. According to Choosing Wisely 76 or older with diabetes are in their A1c target range; the rest are too tightly controlled. This compares to an average of 10 out of 30 of these wide who are most successful (top 10%) at keeping their older diabetic patients' A1c within target range. If you would like more information:

Join your colleagues in Choosing Wisely by:

- Reducing prescription of diabetes medication for older patients
- Using metformin, only (if clinically appropriate)

BE-EHR

- Campaign emails



BE-EHR

- Intervention delivered electronically
 - ▶ engagement with providers at opportune moment
 - ▶ communication triggered by automated evaluation of patient status
- Embedded within the health system
 - ▶ incorporate into existing clinical workflow
 - ▶ minimize burden on busy clinicians
 - ▶ enhance management within context of care
- Waiver of consent for patients
- Outcomes measured using EHR data
 - ▶ CW compliance based on recent HbA1c

Overview

Pragmatic Trials

Digital Platforms

Examples

EMPOWER

BE-EHR

Summary

Summary

- Interventions automated and delivered electronically
 - ▶ low to no burden on providers
 - ▶ minimal reliance on research staff
- Embedded within the health system
 - ▶ incorporate into existing clinical workflow
 - ▶ minimize burden on busy clinicians
 - ▶ enhance management within context of care
 - ▶ minimize information processing by providers
- Outcomes measured using EHR data
 - ▶ reduce burden on participants
 - ▶ reduce burden on providers

Summary

- Enormous potential for innovation
 - ▶ technology
 - ▶ detailed and immediate information
 - ▶ understanding of human behavior
 - ▶ rapid-cycle innovation
- Optimized interventions
 - ▶ must be rigorously tested
 - ▶ must address needs of various populations
 - ▶ must incorporate multiple partners
 - ▶ participants
 - ▶ providers
 - ▶ community health linkers
 - ▶ other social partners

Acknowledgments

- Acknowledgments
 - ▶ Penn *Way to Health* team
 - ▶ David Asch, MD, MBA
 - ▶ Kevin Volpp, MD, PhD
 - ▶ Laurie Norton, MA
 - ▶ NYU EPIC team
 - ▶ Paul Testa, MD
 - ▶ Judd Anderman
 - ▶ Christina Wong

Questions?

